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NEUROPATHOLOGY

OUTLINE

BY

E. E. SOUTHARD

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E. E. SOUTHARD

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OUTLINE OF NEUROPATHOLOGY.

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OUTLINE OF NEUROPATHOLOGY.

I. INTRODUCTION.

The lesions of the nervous system in man are reviewed herein from the side of pathological diagnosis. But few of the data concerning normal nerve tissue are presented, and these incidentally. In a separate chapter I have pursued recent writers beyond our present basis of induction into the field of the neurone theory.

Following is a partial list of books which may be consulted:

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MOTT. Pathology of the Nervous System, in T. H. GREEN, Pathology and Morbid Anatomy. 1900.

NISSL. Nervensystem, Mikroskopische Technik der Untersuchung, in Encyklopädie der mikroskopischen Technik, EHRLICH, KRAUSE, MOSSE, ROSIN, WEIGERT. 1903.

OBERSTEINER. Anleitung beim Studium des Baues der nervösen Centralorgane. Latest edition.

OPPENHEIM. Diseases of Nervous System, translated by Mayer. 1904.

SCHMAUS UND SACKI. Pathologische Anatomie des Rückenmarks. 1901.

II. GROSS LESIONS OF THE NERVOUS SYSTEM.

I shall first discuss the inferences which may be drawn from changes in the nervous system of gross character (size, shape, color, consistence) and follow with a consideration of these changes grouped according to their origin (maldevelopment, circulatory disorders, trauma, inflammation). The pia mater is treated together with the central nervous system as its nutrient membrane.

NUMERICAL DATA.

Average weight of male adult brain	1,358 gm.
Average weight of female adult brain	1,235 gm.
Average weight of brain at birth	383 gm.
Average capacity of male cranium	1,500 cm^3.
Average capacity of female cranium	1,300 cm^3.
Specific gravity of brain substance	1.040
Specific gravity of cord substance	1.034
Specific gravity of nerve	1.034–8

Adult skulls with a capacity of less than 1,300 cm^3. are termed nannocephalic. The intermediate capacities are termed: 1,300–1,400 cm^3., emmetrocephalic; 1,500–1,699 cm^3., encephalic. The length-breadth index is the most commonly used of the cephalic indices. The length is taken between glabella and external occipital protuberance; the breadth, between the points farthest apart in a frontal plane. The formula of the length-breadth index is

$$\frac{100 \text{ x breadth}}{\text{length}}.$$

$$\text{Thus } \frac{100 \text{ x } 14.6}{19} = 76.8$$

Such a length-breadth index places the skull in the mesocephalic series. Skulls with indices lower than seventy-five are dolichocephalic. The brachycephalic index is eighty or higher. Presence of the soft parts about the skull produces an index two to three units higher. The length-breadth index averages about eighty.

The cortex of man averages 2.94 millimeters, of woman 2.91 in depth. The cortex of the left hemisphere is a trifle deeper than that of the right. The occipital cortex is somewhat shallower than the rest.

ALTERATIONS IN SIZE.

An increase in size due to true hyperplasia of the normal elements is unknown. General increase of the neuroglia elements produces in the end a loss of volume by contraction. Apparent increase in size is produced by edema of the pia, by edema of the substance, by hemorrhage, by tumor, and by internal hydrocephalus. The most striking enlargements are seen in congenital internal hydrocephalus, or in any ventricular dilatation produced before union of the cranial sutures. In these cases the dilatation of the ventricles occurs at the expense of the brain substance, so that the total volume of the cerebral substance may be decreased.

Obvious reduction of size occurs, along with characteristic alterations of shape, in the maldevelopments. Senile atrophy, general paresis, epilepsy, porencephalic defect, trauma, may show marked diminution in total mass.

Considerable increase in diameter of the spinal cord is brought about by dilatation of the central canal (hydromyelia), edema, hemorrhage (hematomyelia), tumors, and by dilatation of long fusiform cavities in the substance (syringomyelia).

Notable apparent increase in size of the lower portion of the central nervous system is shown in various degrees in spina bifida. Patent reduction in diameter of the spinal cord is shown in atrophy, notably in tabes dorsalis and in long-standing combined system diseases.

ALTERATIONS IN SHAPE.

Besides the obvious changes in shape effected by trauma and the encroachment of certain external lesions (osteophytes of the calvarium, endotheliomata of the dura mater, cholesteatoma, internal hemorrhagic pachymeningitis, metastatic tumors, inflammatory lesions of skull and dura mater), the brain shows characteristic changes of shape from many internal causes. The most common of these changes is flattening of convolutions as a consequence of heightened tension in the ventricles (internal hydrocephalus) or of generally heightened tension from the presence within the cranium of any lesion or substance which largely reduces the cranial capacity (tumor, hemorrhage, inflammatory edema).

The agency which effects flattening of convolutions may also occasion the cerebellar compression-ring from pressure upon the rim of the foramen magnum.

Opposed to the flattening of the convolutions is the narrowing of the convolutions and correspondent widening of fissures seen in senile atrophy and in local atrophies of various cause. In old age the narrowing of convolutions is a part of a more general process of atrophy, and is consequently attended by internal hydrocephalus; the increase of fluid both in the ventricles and in the meshes of the pia is compensatory (hydrops ex vacuo) to fill space in the cranial box.

From hydrops ex vacuo must be distinguished the edema of the pia of inflammatory or mechanical (in some cases cardiorenal) origin. In the latter there is no great change in shape of the brain.

Besides the general changes in shape there are obvious changes due to local contained lesions. Many of these are more evident in the isolated brain; masses of hemorrhage, abscesses, infarctions, and necrotic tumors may rupture through the pia mater upon the artificial release of tension in removing the brain.

Wide variations in the contour and complication of the gyri are still normal. Cerebral hemispheres differ widely in the development of smaller fissures and annectent gyri. From these slighter deviations from the mean, it is not possible to induce anything with respect to mental or other capacities of the subject.

Well-marked asymmetries, approximations to the smooth brains of the lower animals, and undue richness of convolutions (microgyria) occur both generally and focally.

Of the changes in shape through loss or absence of parts, one of the most characteristic is porencephaly, a condition of local funnel-shaped defect, often in the central portions of a hemisphere, of which many degrees occur up to complete fenestration of the lateral ventricle. Porencephaly and kindred defects and local atrophies follow obstetrical and other injuries, with or without infectious complications, or may be the effect of thrombosis, embolism, or vascular changes, with incomplete repair.

There is a large series of characteristic alterations in shape of developmental or intra-uterine origin. The cases of agenesia of the nervous system range as a rule from the higher more inclusively to the lower mechanisms. The agenesia may consist in almost complete absence of coördinating mechanisms, seen in the monsters (acrania, anencephaly, cranioschisis, craniorachischisis).

The lesser grades of agenesia and aplasia exhibit maldevelopment of the higher (phylogenetically newer) mechanisms, so that the brains more or less approximate those of the lower orders of vertebrates.

Still more complex are the cases in which the external aspect and contour of the brain is preserved, but in which the cerebral substance is in places quite absent, or so thinly deposited that the ventricular fluid is visible through the transparent pia and ependymal lining.

In epilepsy (both in genuine chronic cases and in the Jacksonian type) are often found focal changes of shape (local microgyria or macrogyria) some of which are probably of traumatic origin (from evident involvement of overlying tissues), but others of which remain unexplained.

ALTERATIONS IN COLOR.

The coloring of the uncut brain varies obviously with the amount of contained blood and the state of its hemoglobin. It is not so much the blood in the sulcal veins which modifies the general hue as the blood in the superficial cortical vascular system. Probably the deepest diffuse hues have been observed in fatal cases of malaria. The diagnosis of intracranial congestion is, however, rarely justified on post-mortem evidence merely. Local blood-containing lesions are striking enough.

Besides differences due to blood content, the brain shows variations in grayness and opacity which are of importance in detecting chronic alterations. There must be distinguished a heightened opacity due to thickening of the superficial glia and the focal or general opacities due to changes in the pia mater. The pial opacities are as a rule focal and are most prominent as linear markings over the veins of the sulci, notably on the vertex and along the Sylvian fossæ. The pial opacities may be quite general; but in this case the general thickening which gives rise to them is obvious. An unusually extensive system of arachnoidal villi may be confused with pial thickenings. Flecks of fibrin in edema of the vertex and miliary or conglomerate tubercles are sometimes confused with the opacity due to pial thickening. The heightened opacity due to changes in the subpial glia is more general and less easy to make out with the eye alone.

Dustlike pigmentation is often noted on the ventral surface of the cervical pia mater. Delicate white calcareous plaques in the spinal pia can in appropriate cases be confused with tubercles.

The color of the cut surface shows a series of changes dependent on the content of blood. Puncta cruenta due to venous injection are to be distinguished from perivascular hemorrhages; from the latter the blood cannot be removed by squeezing. Attention to the shade of gray and the variations in translucence will often suggest a minute search for glioses which would otherwise remain unnoted. Light may be thrown in the fresh organ upon the state of the fiber systems by scrutiny of the concentric white markings of the cortex, best shown in the occipital and central regions. Focal differences in color and translucence aid in the gross diagnosis of multiple sclerosis, glioses of whatever cause, tabetic and general paretic lesions, and heterotopia. With respect to heterotopia the possibility of manipulative dislocation of the tissues must be rigidly excluded; no other tissue of the body (except perhaps the diffluent acute spleen) is more subject to artefact by handling than the spinal cord.

ALTERATIONS IN CONSISTENCE.

Palpation of the brain and cord is made as far as possible in situ. Freezing and thawing, formalin injections, delay of many hours before autopsy, and careless removal of calvarium and spines make judgments of consistence difficult. It is especially hard to estimate a diffuse or general increase or loss of consistence. Local differences are readily determined; but the amount of connective tissue framework normal to the region must be borne in mind (thus the motor convolutions are normally wider than the occipital, and the cerebellum is almost always firm on account of its closely set lobes).

Diffuse or general increase of consistence is found in senile brains, together with atrophy of convolutions and compensatory edema of pia. A general increase of consistence accompanies the flattening and heightened resiliency of convolutions found in chronic or acute internal hydrocephalus and in cases of intracranial tumors and foreign bodies. Diffuse or general loss of consistence occurs in cases of edema of the substance. The diffluent substance of the brain and cord found after a varying period post mortem should not lead to diagnosis of non-inflammatory softening. Such diffluence almost always renders neuroglia staining unsatisfactory; but the myelin sheaths retain their staining capacity longer. The brain before and long after birth is soft and watery.

Gross judgments can readily be made of focal differences in consistence. Coördinate parts of the nervous system are compared. Focal increase of consistence is readily made out, for example, in atrophied optic nerves, in the gliosis of the dorsal columns of the cord in tabes, in the multiple sclerosis of children, in some cases of epilepsy, and very markedly in many cases of general paresis. Focal reduction of consistence is found in edema of various origin.

MALDEVELOPMENT.

Gross malformations of the nervous system are largely related to defective development in the posterior median line. The neural groove may fail to form the neural canal altogether (*craniorrhachischisis*), above (*acrania*), below (*rachischisis*).

Acrania may or may not co-exist with absence of brain (*anencephalus*). The brain may be represented by a mass of the usual shape, but unduly small (*micrencephalia*). Or the brain substance may be thinly spread over dilated ventricles which may contain several liters of fluid (*congenital internal hydrocephalus*). The cranium may be in part absent, permitting the brain and its membranes or the membranes alone to herniate (*encephalocele, meningocele*).

A similar series of malformations occur in the spinal system, where through rachischisis a number of structures are permitted to herniate and form voluminous skin-covered swellings (*spina bifida*). *Hydromyelia* is a dilatation of the spinal central canal, the analogue of internal hydrocephalus above. If the cord lies in its usual place, there may take place a dilatation and thinning of its posterior wall with hernia through the defective lumbosacral arches (*syringomyelocele*). Much more commonly the intact cord is carried posteriorly across the hernial sac to be attached to the wall of the cyst, which becomes dimpled or biscuit-shaped thereby (*myelocele*). If the central canal of such a translocated cord becomes dilated, hydromyelocele (*myelocystocele*) ensues. It is plain that surgical interference may be dangerous where cord substance lies immediately beneath the skin, but that a simple meningocele or dilated and herniating arachnoid membrane may be more favorable for operation.

Dimples, sinuses containing hairs (*pilonidal sinuses*), and cysts may develop in the median line above the anus from remnants of the posterior end of the neural groove. These structures have no relation with the spinal canal, which is, as a rule, perfectly developed.

DISORDERS OF CIRCULATION.

Emboli of a diameter large enough to lodge in the circle of Willis itself may do no harm. Smaller emboli occlude the terminal arteries given off from the circle (preferably branches of the left middle cerebral artery), and produce areas of softening (necrosis and local edema) which are often palpable from without or discernible on section. Multiple fat embolism may be found following fracture of the long bones. Air embolism and tumor embolism occur.

Arteriosclerosis gives rise, by slow occlusion or by permitting thrombus-formation in various arteries, or by rupture, to similar and often multiple areas of white or red softening.

The areas of softening (encephalomalacia), whether of embolic or local origin, become somewhat rapidly pigmented in case they contain blood. The surrounding yellow zones gradually fade as the lesion grows older, the edema subsides, the loss of substance is only partially made good by organization, and the typical cyst of softening ensues, with its loose-fibered wall and brownish slightly turbid enclosed liquid. The cysts which follow white softening contain a colorless and almost clear fluid.

Aneurysms (preferably in the basilar and Sylvian arteries) occur and may remain undiscovered in the mass of subpial or subdural hemorrhage following their rupture. Miliary aneurysms should be searched for like miliary tubercles by teasing out and washing the vessels (for instance, the Sylvian arteries).

Voluminous hemorrhage (apoplectic) follows rupture of sclerotic arteries in the brain substance. The most frequently affected of the cerebral arteries is one of the lenticulo-striate branches (Charcot's artery of hemorrhage) of the central ganglionic system.

Edema of the brain, flattening of the convolutions, and pressure about the veins follow; in many cases bleeding continues till the adjacent ventricular wall breaks and all the ventricles are speedily flooded. In other cases coagulation interposes, and a smaller local lesion remains which heals more after the fashion of an infarct. The importance of this typical apoplectic hemorrhage in the basal ganglia depends upon its effect on the fibers of the internal capsule. Thus, if the hemorrhage destroys the fibers of the anterior two-thirds of the posterior limb of the internal capsule, that is, resects the pyramidal tract, total hemiplegia of the opposite side of the body is sure to ensue. Smaller hemorrhages may pick out smaller fiber-systems, whereas larger hemorrhages may involve the upper sensory tracts as well as the motor tracts. At the time of the injury the effects of the hemorrhage are magnified by the surrounding edema; if healing takes place, the lesion diminishes in volume and fewer muscle groups and sensory areas are involved than at the outset. Cured or repaired hemiplegies may live for years and die of some intercurrent disease, often related, however, to advancing arteriosclerosis.

Besides voluminous hemorrhage due to arteriosclerosis, the brain and the cord exhibit multiple small hemorrhages in perivascular spaces which are due to manifold causes. Some of them are due to miliary aneurysms, some to sclerotic changes occurring in the distributing system of arteries, some to whatever conditions underlie the hemorrhagic diathesis, some to the toxines of acute infectious diseases (Staphylococcus pyogenes aureus, Bacillus typhosus), some to electric and mechanical shocks, and some possibly to unknown endotheliolysins. Hemorrhages, in part of mechanical origin, occur in leukemia, especially the lymphatic form.

There are few cases in which it is warrantable from brain findings alone to assert cerebral hyperemia or anemia. This is not to say that they do not occur in life.

In this place may be mentioned two diseases of the dura mater which are of immediate importance. Chronic internal hemorrhagic pachymeningitis consists in the successive deposit and organization of layers of hemorrhage in the inner meshes and on the inner surface of the dura. The pigmented membrane or the fresh hematoma may extensively compress the convolutions, shoving them away from the dura *en masse* with a broad wave-like surface. The condition occurs chiefly in old men.

The sinuses of the dura mater are the site of thrombosis. Marantic (autochthonous) thrombosis occurs frequently in the longitudinal and lateral sinuses of the very young and the old and in chlorosis. In the brain follow stasis, edema, hemorrhages, or even encephalomalacia. The seat of infective thrombosis is, as a rule, the lateral sinus opposite the sigmoid fossa of the temporal bone (following otitis media and interna).

Disorders of the lymph circulation are mainly shown in the ventricles and in the arachnoidal villi. Obstructions in the choroid circulation, notably in the vein of Galen, are often attended with internal hydrocephalus; but, as a rule, chronic inflammation or other occlusive change is found lower down in the ventricular system. Such mechanical obstruction at the foramina of Monro, the aqueduct of Sylvius, and at the foramina of Magendie and Mierjejewski will separately produce ventricular dilatation above the point of occlusion, provided that the lymph transudes as usual from the choroid plexuses. Below the lesion (tumor, organization of exudate in healed cases of meningitis and fracture of the base) the lymph flows away unimpeded to the subdural sheath of the spinal cord.

The circulation in the arachnoidal villi is impeded in chronic passive congestion of the sinuses. In certain cases the arachnoidal villi are themselves filled with blood. Their development varies, although irregularly, with age. In old subjects the villi may form a dense mat a few centimeters wide on both sides of the longitudinal sinus. Some villi grow very large and, sometimes devoid of dural sheath, lie in small cavities in the inner table of the parietal bone; such villi have been known to perforate the bone. They must be distinguished from multiple small true herniæ of cerebral substance, which are occasionally seen.

TRAUMA.

The effects of fracture at the base of the skull (more common than vault fractures) are obvious. Laceration of the temporal lobes is frequent. Hemorrhage occurs at the site of the injury, but is apt to be more extensive, through contrecoup, in the tissues of the quadrant opposite to the injury.

The cases of brain hemorrhage without fracture permit more errors in diagnosis. Not every brain hemorrhage in a case of appropriate accident is due to the accident. Fresh hemorrhage from organizing chronic internal pachymeningitis is a somewhat frequent source of confusion; the subject falling from his hemorrhage produces external injuries which favor the diagnosis, fracture. Rupture of Sylvian aneurysm, apoplexy from arteriosclerosis, hemorrhage from encephalitic lesions, may be hastily interpreted post mortem, as sometimes necessarily in life, to be the effect of trauma.

The result of healed fractures of the skull may become manifest after years. A serious outcome is a slowly condensing scar at the base of the brain producing pressure-atrophy of nerve trunks, and in the roof of the fourth ventricle, affording a chance of the onset of chronic internal hydrocephalus. The minuter lesions in laceration of the cerebrum, whether present alone or in combination with actual fracture, may give rise to protracted delirium during healing. After these lesions, which are in the area of the cortical arterial system, are quite healed (cicatrix, gliosis), they may still give rise to epileptiform attacks. In such cases minute gross search is required for healed lesions.

The effects of trauma on the spinal cord are for the most part obvious. In the peripheral nervous system marked retraction may occur from the point of lesion. Cicatrization (interstitial neuritis) may be complicated after amputation by the occurrence of large bulbous masses (*amputation neuroma*).

INFLAMMATION.

Bacteria invade the nervous system and the pia mater by infective emboli (lung, heart valve, general infection), sinus-thrombosis (otitis media and interna, emissary veins), extension through lymph channels (nose, sheath of optic nerve, perivascular sheaths), and direct extension (dura mater and cranium). The animal parasites (cysticercus cellulosæ, echinococcus hydatidosus) are found in lymph spaces or in the ventricles.

The massive abscesses, derived by extension from the middle and internal ear and found in the temporal lobe and the cerebellum, are unmistakable. They are usually due to the pneumococcus, and are often of long standing and encapsulated. The foci of greatest destruction seem often to occur in the little-nourished area of the white matter of the temporal lobe between the termini of the cortical and the ganglionic arterial systems.

No other massive lesions are as a rule confused with otitic abscess. Large solitary tubercles and gummata require microscopic diagnosis. The findings in other organs are important here.

More characteristic are the miliary tubercles found in disseminated tuberculosis, either separately or in the fibrino-purulent exudate at the base of the brain. The miliary and conglomerate tubercles are often found on the Sylvian arteries, in the choroid plexus, and on the cerebellum, but more sparingly in the vertex. The gross differentiation between tuberculous and granular ependymitis is sometimes impossible.

Diffuse lepto-meningitis is unmistakable. The streptococcus may be recovered from what looks like a slightly turbid edema of the pia. The fibrino-purulent type of tuberculous meningitis may resemble, in the absence of careful search for tubercle, an acute meningitis due to the pyogens.

Leptomeningitis due to the meningococcus shows in very acute cases little exudation, except at the base; the surface of the brain is pink, the pia is edematous, and the beginnings of the exudate appear as yellowish lines along the sulcal veins. The exudate later becomes very fibrinous and is most marked as a rule at the base of the brain, in the cerebellar meninges, and near the fissures of Rolando. The spinal exudate is less in the pia than in the subarachnoid space and is most marked posteriorly. The fluid of the ventricles is increased and cloudy; the ependyma soft, lusterless, uneven. The exudate is apt to extend along the optic, trigeminal, facial, and auditory nerves.

The lesions of leptomeningitis due to the pneumococcus, staphylococcus pyogenes aureus, and streptococcus are rarely so extensive as the meningococcal lesions. The cord is not so extensively attacked, and the nerve roots are spared. Microscopic examination is necessary to distinguish all the forms, with certainty.

Whereas massive abscess and various types of leptomeningitis are grossly striking, it may be hard to distinguish clearly the smaller lesions of acute diffuse encephalitis, meningo-encephalitis, and ependymitis. The small pyogenic abscesses (ineptly likened to flea-bites) may be hard to tell from perivascular hemorrhages. The larger pinkish edematous areas are often confused with areas of encephalomalacia of embolic or thrombotic origin.

The pyogenic abscesses are in fact often hemorrhagic. Bacteria (Staphylococcus pyogenes aureus, Bacillus typhosus) sometimes occasion extensive hemorrhages in the cerebral substance, which may break into the ventricles and present the picture of an apoplexy of arterio-sclerotic origin.

The gross picture of chronic leptomeningitis is well defined. The vertex rarely shows more than small linear plates of thickening over sulcal veins. The tissues at the base show considerable thickening. In many cases the openings in the roof of the fourth ventricle have become occluded by scar tissue, the outcome of organization of exudate there. A frequent outcome of this occlusion, favored by chronic changes about the choroidal vessels, is dilatation of the third and lateral ventricles (chronic internal hydrocephalus).

Changes in the cortex beneath the exudate in cases classified as leptomeningitis, although grossly invisible while acute, can give rise to small adhesions which prevent the pia from stripping readily.

Similar cortical adhesions of great number and extent are found in the brains of general paresis of the insane. Earlier stages may be seen in tuberculous meningitis and in syphilitic meningitis.

Adhesion between dura and pia occurs seldom (except where normal about transarachnoidal vessels and arachnoidal villi); it may occur in extensive trauma, over tumors, and as a healed syphilitic lesion.

The dura mater of children is adherent to the calvarium. Old subjects often show adhesions of varying extent over the vertex opposite the bregma (chronic adhesive pachymeningitis). The dura of the cervical region of the cord is at times locally much thickened, so as to resemble a fibrous tumor; the chronic inflammation involves also the pia mater, the nerve roots, and even the cord septa (*pachymeningitis cervicalis hypertrophica*). The origin of the process is doubtful.

INTERPRETATION OF GROSS APPEARANCES.

It is difficult to interpret the gross appearances of the nervous system in disease. The visible and tangible data in the peripheral nervous system are confined to solutions of continuity, frank atrophy, interstitial neuritis, and involvements by extension from other lesions; many of the most essential changes escape detection. Relatively more can be seen by gross methods in the retina than elsewhere at the periphery. The data of muscular atrophy and apparent hypertrophy should be considered amongst peripheral data.

The gross data of the central nervous system permit in part immediate and certain interpretation. Thus the solutions of continuity in the brain and cord, voluminous effects of vascular disease (sclerosis, aneurism, hemorrhage), massive abcesses, many cases of acute and chronic meningitis, the effects of heightened intracranial pressure, edema, internal hydrocephalus, certain tumors, and various aplasias and maldevelopments permit diagnosis on inspection.

Another series of data becomes clear when considered together with findings elsewhere in the body: thus metastatic tumors, the results of pyogenic and other infections, tubercles, gummata.

There is a great residuum of cases in which the diagnosis must be left in doubt from gross findings. As an example may be cited the diagnosis of glioma. Experience shows that little can be told from the site, size, shape, color, consistence, and other gross characters of a tumor-like mass in the brain, what kind of tumor it may be, or even whether it be a tumor. Brain tumors have in the gross been confounded with tubercles, with gummata, with lesions in a stage of repair, and with areas of hemorrhage, and contrariwise. And tumors have been found microscopically where no tumor was expected from gross appearances. The gross diagnosis of glioma is often successful, but only because gliomata are common. It is, in general, hazardous to predict glioma from gross appearances, and equally hazardous to predicate anything else in the test case.

It is hard to lay too much stress on the mistakes of diagnosis produced by the artefacts made in removal and inspection of the nervous system. The mistakes due to this cause extend into the region of microscopic diagnosis. The fascicular structure of many parts of the nervous system readily permits the most varied and gross translocations of tissue and apparent heterotopiæ which are not interpretable in microscopic sections. Moreover, the size and heterogeneity of nerve cells make them easily accessible to apparent lesion through artificial pressure. Post-mortem changes are of less importance in this matter, although the data as to consistence are disturbed. Then follows a series of artefacts produced, like many in other organs, by the fixatives employed. Reliance is nowadays placed upon total immersion in a solution of formalin or upon various methods of embalming the nervous system in situ. The results and the extent of some lesions are well studied in this way. Many data concerning causes are, however, lost.

III. MINUTE LESIONS OF THE NERVOUS SYSTEM.

METHODS OF EXAMINATION.

The pia mater, vessels, and connective tissues are examined by the methods employed for other organs. Fixation in Zenker's fluid, paraffin imbedding, and staining with methylene blue and eosin form a good method at the outset. The staining with methylene blue and eosin is supplemented by the aniline blue connective tissue stain (Mallory). Arteriosclerosis is so large a factor in many lesions that the elastic tissue stain of Weigert must frequently be used.

For the study of the neuroglia and ependyma, fixation in Zenker's fluid permits the use of the phosphotungstic acid hematein method (Mallory). Weigert's stain for neuroglia may be employed. These methods will not succeed unless the tissue has been fixed within a few hours post mortem. Fibrin stains and the iron hematoxylin method may be employed. The study of the cell bodies of neuroglia cells is best carried on in sections stained with methylene blue and eosin.

The study of the nerve cells may be adequately made with sections stained with methylene blue and eosin after fixation in Zenker's fluid. Excellent work is done with the classical method of Nissl (alcohol fixation, staining with methylene blue soap solution), and, for work on nerve cells which depends for interpretation on comparative studies in the literature, Nissl's method should be used. The manifold methods used by histologists in making clear the structure of the nerve cell are unfortunately of little avail in pathological work, as their results are too precarious or require perfect fixation or are by their nature capricious. The Golgi method, for example, yields few usable data in neuropathology.

Work upon the adnexa of the nerve cell will, as a rule, require fixation in formalin. The data of fatty degeneration are gotten by the Marchi method. The presence or absence of the myelin sheath is determined by Weigert's method for myelin. The axis cylinder and its fibrillæ are as yet scarcely accessible to extensive pathological work. The presence of axis cylinders can be made out by the use of several of the methods mentioned above.

The methods employed fall into two classes according to the desire of the worker to study — on the one hand the cause and nature of the lesions, on the other hand the extent of their effects. It is the effects in tract degeneration which, as a rule, engage neuropathological attention.

PIA MATER AND CONNECTIVE TISSUES.

The thickness, texture, and closeness of attachment of the pia mater should be noted. Judgments of thickness must be modified with the direction of the section, as planes tangential to the cortex cut broader areas of pia. Thickening is usually best marked in the outer layers. The cells of exudations resemble those elsewhere, save that the pigment-bearing or cell-containing phagocyte occurs very early in large numbers. The phagocytes accumulate in lesions of the most varied origin. Mitoses in endothelial cells are found. The forms known as compound granule cells are frequent, containing various products of degeneration of cell, fiber, and myelin.

In acute lesions the amount of edema and fibrin varies greatly. The amount of edema of the pia depends somewhat on the degree of internal hydrocephalus. There is considerable fibrin in exudates due to the meningococcus and the pneumococcus. The intima of the arteries shows proliferative changes in syphilitic, tuberculous, and pneumococcal meningitis, more rarely in other forms.

In chronic lesions the collections of lymphoid and plasma cells about the vessels, especially about the veins, become prominent. These collections are characteristic only in combination with other lesions, such as tubercles, gummata, and the destructive nerve cell changes and proliferative glia changes in general paresis.

About the smaller vessels in the cortex it is noteworthy that the plasma cells readily assume a flattened shape.

Many hardening fluids cause apparent dilatation of perivascular spaces, resembling similar spaces about nerve cells.

NEUROGLIA AND EPENDYMA.

The cells of the supportive neuroglia have round or oval nuclei according to their situation among loose or stratified fibrillæ. The cell bodies are scarcely evident either in normal supportive neuroglia or in the overgrown neuroglia in a reparative or compensatory lesion (lining of old cyst of softening, posterior columns in advanced tabes dorsalis). In stains for intercellular substance (Weigert's or Mallory's neuroglia stains, Mallory's aniline blue connective tissue, iron hematoxylin) the fibrillæ are shown to be everywhere free from the cells, which appear as free nuclei, crossed and recrossed by separate fascicles of straight or smoothly curving fibrillæ, each of one diameter throughout. The number of fibrillæ to a cell is indefinite; it is usually impossible to say whether or not a fibrilla belongs to a given cell. The number of fibrillæ, and to a certain degree the number of corresponding nuclei, is normally greater in the sulci than over the surfaces of the gyri. In the subpial layer of the cortex cerebri it is difficult to estimate the thickness of neuroglia to be termed a lesion. False estimates based on sections made through shallow sectors of cortex must be avoided. There is an increase of thickness of the subpial glia with advancing age.

Where the neuroglia is still actively growing the cell bodies are visible. The nuclei may be larger and clearer, and are, as a rule, eccentrically placed in the cell. Two or more nuclei are not seldom found in a cell. Where the fibrillary intercellular substance is not too dense, the cell bodies may be seen to have processes, so that the cells roughly resemble ganglion cells. The cell bodies are, however, homogeneous and contain no granules. The cell processes are often branched and end bluntly. Along their edges may occasionally be seen fibrillæ which are apparently in the act of separating from the cell. It is such cells which, from their appearance in Golgi impregnations, have been termed spider cells.

In the nerve cell layers the neuroglia cells are rarely found increased without corresponding changes in the nerve cells. Sometimes in the cortex in general paresis the neuroglia cells far outnumber the nerve cells. The age of foci of gliosis can be roughly told from the presence, in acute lesions, of mitotic figures, multinucleate cells, and cells with branching processes; in later lesions of cells with fibrillæ apparently in the act of splitting off from processes, and cells with smaller cell bodies in whose neighborhood the fibrillæ outnumber the processes, and, finally, of fascicles of fibrillæ in which relatively few apparently free nuclei are imbedded. The mitoses of endothelial cells, so frequently found in destructive brain lesions which are still active, may sometimes be confounded with true neuroglia mitoses. In the pineal body, in places where the neuroglia abuts upon nonnervous tissue (adventitial and pial connective tissues) in gliomata, at the edges of old cysts of softening, and occasionally elsewhere, much larger and strap-shaped fibrillæ are found. In appropriate places these fibrillary masses may be shown to fray out at the ends like cut wire rope. Some of the structures described as neuroglia feet applied to vessels can be resolved into such structures.

The ependyma is often desquamated, especially from the tops of the elevations in granular ependymitis and in edema of the ventricular walls. Over areas from which the ependymal layer has been absent for some time there occur focal fibrillary overgrowths of neuroglia. With advancing hydrocephalus these focal accumulations of cells and fibrillæ condense and are projected farther and farther beyond the ependyma layer to form the grossly evident granules of granular ependymitis. This condition is perhaps wholly a mechanical effect. It occurs in arteriosclerosis, cardiæ, and cardiorenal diseases, as well as in tuberculous meningitis and local brain diseases with increase of ventricular fluid.

Below the ependyma there occur in many diseases, but especially in epidemic cerebrospinal meningitis and in tuberculous meningitis, characteristic multinucleate structures, in whose cytoplasm may be light areas containing numerous dots or short rods which assume the neuroglia stain. Similar structures are seen in the neighborhood of the central canal of the cord, and here numerous fibrillæ run in close apposition to the cell walls.

NERVE CELLS AND ADNEXA.

The nuclei and bodies of all nerve cells may exhibit a series of changes resembling those of the parenchymal cells of many other organs. In the larger cells, which show Nissl granules, the [illegible] riking. In the axis cylinder, myelin sheath, and pericellular structures, there is a series of lesions having few analogies elsewhere in the body.

As to general nerve cell hypertrophy there is no evidence. Atrophy is observed in a variety of chronic diseases, both vascular diseases and some not evidently vascular. Simple atrophy may be made out from small size of the cell, more deeply re-entrant angles between dendrites, apparent increase of autochthonous pigment, absence of dendrites, or absence of axis cylinder connections. In higher grades of atrophy the cell body stains densely (pyknosis) ; but pyknotic or chromophilic cells are often artefacts and, at any rate in human material, do not signify general atrophy. Atrophic cells may become calcified.

Nerve cells undergo *cloudy swelling*, which may be shown by their contours alone, when well-defined swellings appear between the bases of the dendrites. Cloudy swelling is distinguished from *fatty changes* if the granules clear up on the addition of acetic acid. Frozen sections may be stained with Scharlach R. The pigments assume a red which is much less intense than the red given by fat in Scharlach R.

Besides cloudy swelling and fatty changes, nerve cells at times show a degenerative change in which the cell body seems to consist of coarse dust-like granules. In certain cases these granules are fibrinoid, and stain with methods for fibrin and neuroglia.

Vacuolation may be present due to collections of fluid or of colloidal substances. The effect of reagents must be rigidly excluded for the strict diagnosis of vacuolation.

The nucleus may undergo in the course of cell destruction the process of lysis, rhexis, pyknosis, quite as with other cells. Karyokinesis has not been observed. Occasionally there is seen a dense refracting mulberry-like nucleolus, doubtless an artefact.

Besides the relative increase of cell pigment seen in atrophy there occurs an absolute increase of pigment, which may lead to cell degeneration.

In those cells which have large cell bodies containing Nissl granules, and especially in the larger somatochrome cells, there is a series of lesions marked by changes and disappearance of the granules. The granules may become dissolved or fail to stain near the nucleus (central chromatolysis) or in the cell periphery (peripheral chromatolysis) or throughout (total chromatolysis). The granules may undergo dust-like transformation, may fragment, or may be apparently swollen.

These granule changes, although described as specific, are no more specific in various brain and cord lesions than are the more general changes in nerve cells. The whole cell picture must be considered. Of definite and consistent cell reactions, the best example is the axonal reaction (tertiary degeneration) of the nerve cell, which is a rapid outcome of separation or destruction of its correspondent nerve fiber. In the axonal reaction the Nissl granules (of an anterior horn cell, for example, directly after resection of corresponding nerve) fall into fine particles or become dissolved, and permit the nucleus to assume a mural position or sometimes to indent the wall. This condition is often perfectly curable, but may in some cases lead to atrophy.

Marked but curable changes are brought about in fever — swelling of cell and dendrites, disappearance of Nissl granules, with transformation into very finely granular material, disappearance of nuclear outline.

The most celebrated of the alleged changes is the *acute Veränderung* of Nissl. In a case showing this alteration, according to Nissl, every nerve cell of the cortex is swollen. The nuclei are enlarged and round (the normal nucleus of a pyramidal cell is slightly oval). The nucleoli are dark, but contain light points. The Nissl granules fail to stain, or cling as small plates to the nuclear membrane. The cell bodies stain faintly; their borders are indistinct. The dendrites are stained for longer distances than is normal; their bodies are indistinct. The axone hillock, however, stains (contrary to the normal condition) and stains sharply. It is best for comparative purposes to employ Nissl's original method for nerve cell work.

The pericellular net and the neurofibrillæ are brought out quite capriciously with accessible methods. No lesion can be argued from their absence. The pericellular region may show an increase of satellite cells, rarely polynuclear leucocytes, and coagulum. The satellite cells are at times increased in number and may indent or occupy spaces within nerve cells (so-called neuronophagia, neuronoclasia). Deeply staining incrustations are occasionally found on the nerve-cell borders.

With the other adnexa, *i.e.*, the axis cylinder and myelin sheath, the lesions are more definite than in the pericellular net and the intracellular fibrillæ. The axis cylinder and the myelin sheath, as a rule, undergo destruction together. Only in the classical "sclérose en plaques" (multiple sclerosis of adults) do the axis cylinders preserve function in the absence of myelin investment. Just as the nerve cell exhibits a typical axonal reaction on separation from its fiber, so the fiber undergoes degeneration when separated from its cell. The swelling and fragmentation of axis cylinder and varicosities and fatty degeneration of myelin sheath attack the fiber distal to the point of injury and for a short distance proximally. The local destruction due to the trauma (traumatic degeneration) is succeeded in a short period by a secondary or paralytic degeneration of the part separated from the correspondent nerve cell.

MALDEVELOPMENT.

The cells of ill-developed brains differ from the cells of brains which have been subject to lesion by the absence of scar tissue, and gliosis. Nevertheless the injuries may be wrought so early in life that well-marked gliosis is not yet possible. In such cases, for instance in porencephaly, it may be impossible to distinguish from an examination of the cells whether the lesion is the effect of maldevelopment or early lesion. The brains of old idiots form the most fruitful material for study of these conditions. It is sometimes possible in these brains to secure fair imitations of the cortex of lower animals. The cellular structure of the human fetal brain of various stages is reproduced in some cases.

Another series of maldevelopment cases shows not merely absence of parts and stoppage of cell development, but actual distortions and heterotopia of structures. An instance of this is the formation in malformations of the cerebellum of islands of cells resembling Purkinje cells, but without processes, surrounded by a few cells resembling those of the granular layer.

CIRCULATORY DISORDERS.

Anemic necrosis in the brain and cord is of the colliquative form. The dead tissue softens and swells into a mass of gray detritus which may be variously colored by blood. The detritus contains considerable myelin or material staining with osmic acid. Hemosiderin and iron-free pigments may occur in the area. Granule cells rapidly appear, to aid in absorption.

Very small areas of colliquative necrosis may become thoroughly organized. The rule is partial organization, with cyst formation.

The cyst fluid may be yellowish or brownish and slightly turbid, containing numerous fatty granule cells. The walls are uneven from the jutting in of vascular tufts surrounded by coarse and fine neuroglia fibrillæ. The older lesions show a slowly condensing capsule of neuroglia, with fewer and fewer neuroglia cells of the type in which cell bodies are evident.

Small hemorrhages into the brain substance are characteristically linear, dissecting the perivascular sheaths or running between fiber fascicles. In the clot hematoidin crystals and hemosiderin are demonstrable. Dissolved iron-containing pigment may be reprecipitated for a considerable distance from the original extravasation. Phagocytes are found containing blood globules and pigment. Reabsorption of perivascular hemorrhages is rapid; but pigment-bearing phagocytes are demonstrable long after the injury. The process of healing in destructive hemorrhage resembles that of anemic necrosis. Occasionally there may be found in the destroyed area dying nerve cells, whose shrunken bodies contain granules smaller than Nissl granules, and staining by methods for neuroglia and fibrin.

Periarterial overgrowth of neuroglia may be found in cases with normal vessels, in arteriosclerosis, and in gliomata.

Hyaline degeneration is found in the media of small vessels in the brain and in the meninges in tuberculous meningitis and other conditions. This may be hard to distinguish from caseation. Some of these areas are partly calcified.

The intimal changes of arteriosclerosis are frequent. Subendothelial proliferation of intimal cells occurs in tuberculous and pneumococcal meningitis. Rapid and extensive intimal proliferation in meningeal vessels is characteristic of syphilitic meningitis.

INFLAMMATORY LESIONS.

The ending "-itis" is extensively used in describing lesions of the nervous system of quite various origin (thus alcoholic polyneuritis, compression myelitis, parenchymatous-degenerative myelitis, granular ependymitis, traumatic, toxic, and bacterial encephalitis). The ending "-itis" *as used* virtually means "lesion of."

The course of exudation and repair in the nervous system exhibits peculiar features. The passage of fluid from the vessels is peculiarly swift and voluminous; and the edema may at times be remarkably transient. Diapedesis and small perivascular hemorrhages are frequent. The exudation of polynuclear leucocytes, though even and voluminous in the meninges, is somewhat rare in the brain substance itself except in large destructive lesions and in areas softened by edema. The most characteristic cell of various brain lesions is the large phagocytic or compound granule cell which accumulates often in extraordinary numbers about vessels and in cysts of softening. Many of these cells are of endothelial origin; mitoses are often demonstrable near vessels.

Besides the changes in and about the vessels, which nerve tissue shares with other tissues in inflammation, there are changes in the neuroglia of the central nervous system in inflammation. Upon the density of the subpial neuroglia may be dependent the slight penetrative power into nerve tissue which polynuclear leucocytes show. If this subpial glia is dissolved by local lesions, as in epidemic cerebro-spinal meningitis, the leucocytes wander considerable distances from the pial vessels. The leucocytes wander readily in either direction through an apparently intact ependyma. The neuroglia cells in the cortex and beneath the ependyma are increased in number. Mitoses in the glia are demonstrable in favorable cases. Neuroglia cells with large cell bodies, one to several nuclei, and branched processes are frequent. The cells may be so abundant, in cases of epidemic cerebrospinal meningitis, as to outnumber the ganglion cells.

In repair the neuroglia cells pass through the usual series of changes leading to new fibril formation. In case there is no destruction of vessels, the outcome of the process will be an accumulation of neuroglia fibrillæ which at first slowly contracts, but finally remains stationary. The fibrillæ abut endwise upon the vascular adventitia. As they approach the pia they assume two relations thereto: the majority of the fibrillæ are tangential, but a number of parallel fibrillæ touch the pia endwise, sometimes fraying out. The glioses in the lower cell layers are less regular in appearance. By irregular contractions the normal radial arrangement of the nerve cells is distributed. An irregular disposition of glia nuclei can sometimes be noted between the fibers of the white matter.

Acute inflammation of the pia mater is almost necessarily attended with effects upon the substance nourished by the membrane. Pyemic abscesses of cerebrum and cerebellum are also frequently accompanied by pial lesions. Massive abscess is often found without pial lesion; nor is the relation by veins or lymphatics to the ear always demonstrable, even in temporal abscess with coexistent inflammation of the middle ear.

Pyemic abscesses are often hemorrhagic, although lesions in the blood vessels are not always demonstrable. The hemorrhages appear to originate often in the neighborhood of the layer of large pyramidal cells.

REPAIR AND REGENERATION.

The peripheral nervous system exhibits remarkable reparative and regenerative processes after injury. The processes of degeneration following injury are the same as those exhibited by the central nervous system. Thus, besides the local degeneration due to trauma, a characteristic secondary degeneration affects the axis-cylinders and myelin sheaths for their total length distal to the injury. This secondary or paralytic degeneration affects also the central stump as far at least as the first nodes of Ranvier above the point of lesion. The sequel to the secondary degeneration of peripheral nerves, however, differs notably from the slow gliosis which follows secondary degeneration in the central tracts. The peripheral nerves after injury tend to regain function by complete regeneration of their axis-cylinders and myelin sheaths. Anatomically the peripheral nerves differ from central nerve bundles in a lack of supportive neuroglia and in the presence of the sheaths of Schwann.

It is not clear what brings about the regeneration of the conducting elements; it is doubtful whether the axis-cylinders simply repeat in regeneration the course of embryonic growth by growing outward from the point of lesion, or whether they are laid down peripherally by the aid of adjacent elements.

Active proliferation of the cells of the sheaths of Schwann is shown as early as the fourth day after injury, at a time when the fragmentation of axones and myelin is still marked. The regeneration of the axis cylinders follows slowly. The regeneration begins centrally, and where growth is not obstructed proceeds roughly at a rate of one millimeter a day toward the periphery. This direction of growth repeats the embryonic direction, but no similar regeneration takes place into the spinal cord after resection of dorsal roots adjacent to the cord. Peripheral regeneration is favored by the presence of the corresponding motor and sensory cells. The autogenous regeneration of axis cylinders described as occurring in young vertebrates independently of the correspondent nerve cells yields a partial, but never permanent, restoration of function. A regeneration of peripheral nerves, in every sense complete, is effected by a distal new growth of axones and myelin sheaths which is earliest demonstrable in areas nearest the lesion. The axis cylinders of the central stump tend in growing out to split into bunches of smaller fibers. The rate of regeneration depends largely upon the initial character of the traumatic changes. The distance to be travelled by the axone fibrils and the varying density of the cicatrix make it impossible to assign the time of recovery within months. The most convenient tubular path seems to be chosen by the regenerating axones which grow along threads or through hollow objects inserted in the tissue. This tendency is turned to account in the surgical suturing of nerves, wherein reversed segments of the nerve itself are employed to effect union over wide gaps. After amputation curious painful tumors ("amputation neuromata") are occasionally produced by irregular and ineffectual regeneration of axis cylinders within the scar.

In the healing of nerves there is (1) a local scar formation following the traumatic degeneration, and (2) a neurotization of the scar by distally-growing axones, and finally (3) complete regeneration of the distal portion of the nerve. Secondary degenerations in the central nervous system, on the contrary, are healed not by axone regeneration but by gliosis.

PRIMARY DEGENERATION.

The term "primary" not only cloaks ignorance of the cause, but also is frequently applied to conditions of which the early stages have never been observed. Primary degeneration, whatever it be, is contrasted with secondary (paralytic or Wallerian) degeneration, and this in turn with the tertiary degeneration of nerve cells after peripheral injury.

As a rule, however, the term "primary degeneration" is used, not of effects wrought in separate cells, but of effects going forward in several tissues, such as nerve-cells, glia, and sometimes the connective tissues. The effects seen in the glioses of tabes, general paresis, and multiple sclerosis of adults cannot in part be distinguished from the phenomena of repair. In some diseases examined, early signs of the process of degeneration may be found in nerve cell changes, fragmentation and solution of axis cylinder, varicosities, and fatty change in myelin sheaths. But these active changes differ in no point from degenerations whose causes are known.

NEW GROWTHS.

Besides secondary tumors, of which the brain is a frequent site (from *breast cancer*, *malignant chorio-epithelioma*, *melanotic sarcoma*), the nervous system exhibits characteristic primary tumors. The most frequent primary tumor is the glioma which may be soft and cellular (*glioma molle*), hard and rich in fibrillary intercellular substance (*glioma durum*), or supplied with cysts and ependyma-like collections of cells (*ependymal glioma*). Multinucleated cells and cells roughly resembling ganglion cells occur in many examples of glioma. It is not clear that these types are genetically separate. The gliomata of the brain are, as a rule, single, grow by infiltration in nerve tissues (sparing both membranes and cranium), and tend to interstitial hemorrhage and necrosis. There is no evidence that the glioma produces a toxine. The malignancy of gliomata depends on their situation.

Very large tumors develop, often without symptoms, from the dura mater (*endotheliomata*), grow by expansion inwards, shelling out smoothly from deep spheroidal pockets in the cortex. The tumors often contain considerable masses of lime and then constitute the most frequent variety of psammoma.

Sarcomata of the brain (excepting those developed from membranes or cranium) are rarer than has been supposed. The older accounts, in which no study was made of the intercellular substances, form no good basis of statistics. Tumors of the fibrosarcoma group are the commonest variety of sarcoma found.

Cholesteatomata (pearl tumors) are epidermoid tumors, as a rule in close relation with the pia mater or the choroid plexus. They are composed of dead and dying epithelial cells, which are often mixed with cholesterin crystals and accumulate indefinitely. The tumors are dangerous from their site.

The psammoma (tumor containing lime concretions) is a frequent tumor of the choroid plexus, and occurs also in the brain substance and in the pineal body. Microscopic examination is required to tell whether a psammoma belongs to the sarcomata or the gliomata.

Other primary tumors occur. The most prominent of these are angiomata of several types and sarcomata of the type secreting intercellular substances, developed, as a rule, from the meninges.

The *chordoma* is a small tumor which develops from the remains of the chorda dorsalis at the spheno-occipital synchondrosis. The tumor lies at first outside the dura, but later may push its way beneath and attain the size of a cherry. The tumor is mucoid in consistence. There is a homogeneous intercellular substance. The cells are highly vacuolated.

Neurofibromata are fibrous tumors developing from the interstitial tissue of peripheral nerves. Sometimes the new growth takes place from the endoneurium, in which case the nerve fibers run separately through the tumor. Sometimes the perineurium is the starting-point of the growth, in which case the nerve bundle runs through the middle of the tumor. In the larger tumors nerves may no longer be demonstrable. The size of the new growth is not in proportion to the size of the nerve bundle from which it develops. Similar tumors may develop from other structures than nerves.

The spinal cord shows various tumors of the types seen in the brain. The condition known as *syringomyelia* may be grouped with the new growths or with the maldevelopments. In syringomyelia fusiform cavities are found, as a rule in the cervical cord, related with the central gray substance, often of the posterior horns. The cavities are lined with edematous neuroglia and are thus contrasted with the cavities lined with ependyma found in hydromyelia (a dilatation of the central canal analogous to internal hydrocephalus). The origin of syringomyelia is unknown, but probably manifold. Certain cases yield typical clinical pictures.

On account of the number of tissues which go to make up or may be included in the nervous system, few diagnoses of primary tumors can be rendered without resort to methods for demonstrating intercellular substances as well as the cell forms.

IV. DISEASES PECULIAR TO THE NERVOUS SYSTEM.

The central nervous system consists of parallel and interlacing tracts of medullated fibers and of voluminous gray centers interposed between the termini of the tracts. The fiber tracts permit linear conduction only, whereas the gray centers effect, besides an end-to-end conduction between tracts, also multiple cross-conductions, in virtue of which indirectly any two tracts may be made to intercommunicate.

Although the nervous system throughout presents this fascicular structure, yet the bundles are far from being on one level of importance. It is conceivable that no single fascicle of the central nervous system is essential to the performance of its functions, on account of the manifold switching of impulses made possible by cross-conductions through the gray centers. Moreover there is one great group of fiber fascicles which may be quite cut out of function without impairing vital activities — the association tracts of the brain. In fact, in the lower orders of animals no such system is developed.

To the great group of association tracts, which appear to form a specialized apparatus for elaborate cross-conductions between gray centers, may be opposed the group of fiber fascicles known as the projection system (motor and sensory tracts). The fascicles of the projection system are interposed, not between gray center and gray center, but between skin and voluntary muscles or between eyes and glands or between mucous membranes and the sympathetic system, and so on. The fascicles of the projection system serve to unite functionally various non-nervous structures. For a complete projection system but one loop is theoretically necessary with a center for inter-communication. As it happens, however, in man and the higher animals various gray centers are interposed at lower levels, forming shorter loops. These various fascicles between centers are subject individually to disease; and the different combinations of disease which are for some reason confined to the tracts and centers are known as system diseases. The system disease is then, in a sense, a focal disease of the nervous system; but the foci are linear, extensive, not related with the distribution of the arterial tree, anatomically and physiologically well-defined. The neurone theory has been offered as the key to an explanation of these diseases. I have here presented the diseases objectively.

Focal injury to the adult nervous system produces more than focal effects. Remote regions are rapidly involved in what has been termed a secondary degeneration. In a case of focal lesion the tracts showing secondary degeneration will be characterized as follows:

1. The degenerated path runs out of the region of injury and is proportional in number of fibers to the elements of the destroyed area.

2. The area of degeneration does not spread by contact in its course with other areas. In case the degenerated path splits, the total cross-section of degenerated fibers remains the same and the area between remains intact.

3. The process of degeneration shown is at the same stage throughout the degenerated path.

4. The changes in the gray center corresponding will affect only the appropriate cells. Cells of various dignity will not be involved by reason of contiguity.

It is evident, therefore, that regular and systematic remote changes are wrought by destruction of isolated parts of the nervous system. Similar extensive changes of the same general character are found in cases where there is no evidence of destructive lesion of isolated parts of the nervous system. The cause of these extensive fascicular diseases remains unknown. In many examples the history indicates a slowly acting cause. Older writers were content with the degenerations as primary or idiopathic. Modern writers mention poisons elaborated within the body, the persistent toxine of syphilis, or a combination of these as causes for certain forms. A group known as the combined system diseases has been related with pernicious anemia. Repetitions in successive generations have been noted in some forms. The group as a whole scarcely differs qualitatively or presents different logical problems from various chronic diseases of other organs. The peculiarities of the group are the extent of the lesions, their apparent caprice of development at various foci, and the delimitation and constancy with which various functions are modified or removed thereby. Therefore, it has been said, the triumphs of neuropathology lie in applied solid geometry.

Some effects of lesion in various foci are first considered, and the well-marked system diseases follow :

SECONDARY DEGENERATIONS.

1. Cerebral Palsy of Children.

Extensive lesion, such as acute hemorrhagic encephalitis of the Rolandic region, produces as a rule in children convulsions followed by a hemiplegia or unilateral paralysis of the arm and leg, or of the arm, leg, face, and possibly the tongue. Stable contractures or spastic innervation (tendency to tonic contractions in lieu of movement) of the muscles follow. Characteristically also occur associated movements, athetosis (slow, successive contractions of muscle groups, with extension and flexion, adduction and abduction, at short intervals), a degree of imbecility, and a tendency to convulsions on the paralyzed side.

At autopsy the cortico-spinal motor tract will be found degenerated. At successive levels this tract occupies, first, a part of the converging coronary or tegmental radiations of the centrum semiovale, next, the anterior two-thirds of the posterior limb of the internal capsule, and, now as the pyramidal tract, the middle ventral portion of the foot of the cerebral peduncle. In its course through the pons and medulla oblongata, the various bundles corresponding with the cranial nerves diverge to the raphe, decussate, and come into relation with their respective cranial nerve nuclei. The fibers of the corticospinal tract itself continue to the (incomplete) decussation in the medulla. The degeneration in the spinal cord will then be seen in large part in the pyramidal tract of the opposite side, but in small part also in the direct pyramidal tract.

CEREBRAL MONOPLEGIA AND CORTICAL EPILEPSY.

Under the head "cerebral palsy of children," the frequent cause mentioned was hemorrhagic encephalitis. A similar hemiplegia due to cortical lesion fails to occur in the adult. In the adult inflammatory lesions of the cortex are likely to be so extensive as to produce more general signs than hemiplegia; or, if small, experience shows that the signs produced are of limited range. A destructive lesion of the motor cortex produces some form of cerebral monoplegia or paralysis (without atrophy) with contracture and increased deep reflexes of the limb or muscle groups involved. If the lesion be not destructive, but leave the gray center in a state wherein its functions are performed abnormally, a local form of epilepsy (cortical or Jacksonian epilepsy) is produced, characterized by unilateral spasms (bilateral in the case of muscle groups which normally act bilaterally).

Just as in the cerebral palsy of children, a variety of lesions may produce in the adult the local signs of cerebral monoplegia or cortical epilepsy; but in the latter, perhaps the most frequent cause is new growth, though trauma and inflammatory lesions are often found.

In the case of cerebral monoplegia the degenerate tracts may be followed down in the corticospinal tract sketched under cerebral palsy of children. The coronary radiations from the cortex are slowly shifted in their downward course, so that in the cerebral peduncle the fibers from the frontal cortex come to lie internally and the temporal and occipital fibers come to lie externally with the motor or pyramidal tracts set between.

CEREBRAL HEMORRHAGE.

Apoplexy, or cerebral hemorrhage par excellence, is most often due to rupture from disease of a branch of the anterolateral group of the central ganglionic arterial system (branch given off frequently from left middle cerebral artery). The corticospinal motor path becomes degenerate in the cases which recover. Over and above certain general symptoms, the main result is hemiplegia of the side opposite to the hemorrhage. Considerable gradual restriction of the number of muscle groups affected is the rule. Contractures set in, as in the case of cerebral palsy of children and cerebral monoplegia, and atrophies of the correspondent limbs are equally absent. The aphasia, which complicates extensive left-sided hemorrhage, is likely slowly to disappear.

DISEASES OF THE PONS AND BULB.

Glossopharyngolabial (bulbar) paralysis is a name given to several types of disease (the so-called progressive form of beyond middle age, a hereditary form found in children, an acute apoplectic form, a compression type from new growths). It is obvious that small lesions of various nuclei will produce appropriate loss of function and degeneration in appertaining tracts. In the bulb the tracts and the centers are collected into very small compass, so that a lesion the size of a pea may cause bilateral paralysis of, for example, the twelfth nerves. A lesion placed beside the pyramidal decussation produces crossed hemiplegia, involving the fibers of the motor tracts of one side above the decussation and tracts of the other side below the decussation. Contralateral hemiplegia ensues upon lesion above the decussation just as in cerebral palsy of children or in the classical cerebral hemorrhage; but, inasmuch as the destructive lesions must be much smaller so to single out limbs or muscle groups, the history and clinical pictures are likely to be different. These local pontine and bulbar diseases are apt to be chronic. An exception is the form clinically known as the acute apoplectic form, due to basilar thrombosis or to encephalitis (acute polio-encephalitis inferior). Acute hemorrhagic encephalitis confined to the central gray of the floor of the third ventricle and the Sylvian aqueduct (acute hemorrhagic polio-encephalitis superior of Wernicke) produces a bilateral ophthalmoplegia, termed nuclear, with correspondent secondary degenerations in the oculomotor paths in chronic cases.

TRANSVERSE LESIONS OF THE SPINAL CORD.

Transverse lesions of the spinal cord produce pictures of degeneration which differ somewhat at various levels, but have several features in common. Thus, near the plane of lesion, total degeneration of ascending, descending, and commissural tracts is found. At various levels remote from the transverse lesion the tracts degenerate according to a general principle, viz., the motor conducting paths *in general* degenerate downward, the sensory paths *in general* upward.

Below the plane of lesion the pyramidal tracts degenerate, as in the series of lesions just described (cerebral palsy, hemorrhage into internal capsule). In transverse lesions of the upper cord both the crossed and the direct pyramidal tracts degenerate below the plane of lesion. But, inasmuch as the direct pyramidal fibers have all decussated by the middle or lower thoracic segments, below that level the descending degeneration is confined to the crossed pyramidal tract.

Above the plane of lesion (1) a portion of the fibers of the posterior columns degenerate, but, on account of fresh accessions of uncut fibers from higher posterior roots, the area of ascending degeneration continually shifts inward, occupying the column of Goll. (2) The direct cerebellar tracts are degenerated in transverse lesions of the cord which are high enough to cut off the connections between this tract and the cells of Clarke's gray column, which is developed in the median gray of the thoracic cord. But in transverse lumbar lesions the direct cerebellar tract is naturally at no point degenerate.

Of the other tracts of the cord a variety of interesting facts are known. The degenerations of the short and commissural tracts near the lesion are obvious, but not extensive. The degenerations in the long tracts other than those described are difficult to estimate, and particularly difficult to translate into functional terms because the fascicles are composed of a mixture of fibers, some of which are ascending and others descending. The posterior columns show, besides the extensive degeneration above the plane of lesion, also small (in cross-sections comma-shaped) tracts of degeneration below the plane of lesion. The fibers concerned in this descending degeneration are the descending branches of the dorsal root fibers.

UNILATERAL LESIONS OF THE SPINAL CORD.

Stab wounds occasionally produce hemisection of the spinal cord, upon which follows the symptom complex known as Brown-Séquard's paralysis. The anatomical basis of this symptom complex is in part obscure. Paralysis on the side of the lesion is due to section of the direct pyramidal tract. Anesthesia on the side opposite to the lesion is supposed to be due to the section of sensory fibers which decussate immediately after entrance into the cord. But the anesthesia is incomplete, as the muscular sense is intact; accordingly the fibers corresponding with muscle sense are supposed to decussate higher up. Complex but quite definite symptom groups are produced by lesions at various levels. It is impossible, as it would be unwise, to learn these complexes by rote. Only familiarity with the anatomy of the cord and results of experimental work permits diagnosis.

SYSTEM DISEASES.

The conditions sketched under secondary degeneration are the outcome of known destructive injuries. Roughly similar degenerations, in point of extent, are produced in various unknown ways. The best defined of these degenerations occur in tabes, in progressive muscular atrophy and amyotrophic lateral sclerosis, and anterior poliomyelitis. At present, however, anterior poliomyelitis may be ranged perhaps better with the results of bacterial inflammation.

Together with these conditions may be considered the combined system disease and multiple sclerosis.

TABES DORSALIS.

A small percentage of syphilitic subjects five to fifteen years after infection, and a number of other subjects in whom syphilis cannot be proved, are attacked by a disease which early exhibits loss of knee-jerks, Argyll-Robertson pupil (accommodating for distance, but failing to respond to light), lancinating pains in various parts, analgesia usually of the lower extremities, and, perhaps, Romberg's symptom (swaying with closed eyes). Other phenomena are added later and give tabes its other name, locomotor ataxia. The disorder of movement is due, not to weakness, but to incoördination, and usually affects the lower extremities first. The most frequent disease of the cranial nerves is paralysis of the oscular muscles (the only true motor symptom of tabes). The optic nerves often undergo progressive atrophy. Characteristic are disturbances of the joints and bones, malum perforans (perforating ulcer, as a rule, of the sole of the foot), spontaneous gangrene, and other disorders all referable to destruction of the trophic apparatus of the spinal cord. The degenerations of tabes progressively attack various regions of the spinal cord. The initial sclerosis may be quite invisible to the naked eye, as the change is quite narrowly confined to the region of the dorsal root zones of the middle or lower lumbar segments of the cord. The disease is not easily recognized from the gross cord till later stages, in which a flattening and narrowing of the posterior columns of many lumbar and thoracic segments is observed. But in the middle stages it is still possible to make out an increase of consistence and a slight graying-out of the posterior columns examined in cross-section. The stage of the disease is more surely determined by microscopic examination of various cord levels. The older the process locally, the more marked the atrophy and the corresponding gliosis and the smaller the area of degeneration as seen in cross-section. The more advanced the disease, as a whole, the more entering dorsal root fibers are affected, and the wider will be the ascending tracts of degeneration in the posterior columns. It is in this disease that the prettiest demonstrations are afforded of the relationship between the columns of Goll and of Burdach and the lower and higher dorsal root systems respectively. Thus in an early case of tabes dorsalis an examination of serial sections from below upward exhibits the ascending prism of degenerated fibers slowly translocated inward, to form the column of Goll, through the accession of fresh undegenerated fibers from higher nerve roots. In the rare cases of cervical tabes the relationship is reversed. In cervical segments from a case of tabes cervicalis, it is the fibers of the column of Burdach which are degenerate; whereas the fiber system of the column of Goll, derived from the intact roots and ganglia of the lower dorsal and lumbar regions, remains unaffected. However, in the majority of cases of tabes dorsalis, seen at autopsy, the changes are already spread over many segments, and there may usually be seen gross thinning out of the dorsal columns.

PROGRESSIVE MUSCULAR ATROPHY.

Persons in middle life may become subject to a slowly developing disease, which starts with a flattening of the ball of the thumb and a deepening of the interosseous spaces in the hand. Fibrillary twitchings and gradual atrophy ensue. The atrophy overtakes various muscles of the arm and shoulder, not by continuity, but by springing from one group irregularly to another group of muscles. In the course of several years most of the arm, shoulder, and back muscles are atrophied, and the muscle groups which are spared undertake, as well as possible, the functions of the atrophic muscles. The so-called "living skeletons" die of intercurrent disease or are destroyed by an advance of the atrophy upon the respiratory and other muscles controlled from the bulb.

The spinal cord, at appropriate levels, shows a variety of degenerations of which the most constant is atrophy of the anterior horn cells.

AMYOTROPHIC LATERAL SCLEROSIS.

Men of thirty to forty years sometimes become subject to a disease consisting in paresis and contracture of the arms or of all the extremities, in which the muscles undergo atrophy. The disease is apt, later in its subacute course of eighteen months to two years, to involve also the muscles of the tongue, the face, and the pharynx. Death is likely to ensue when the pneumogastric nerve becomes affected.

Nothing is known of the cause of this disease, but the findings in the nervous system are striking. The cells of the anterior horns in the cord at levels corresponding with the muscular atrophies are reduced in number and size, perhaps overpigmented. Especially the large motor cells are affected. The cells of Clarke's column remain intact. The nerve fibers of the anterior horns, the anterior root, and of the direct and crossed pyramidal tracts have disappeared. The area of the crossed pyramidal tract affected is, as a rule, larger than the similar area brought about by secondary degeneration. That the disease is progressive is shown by the occurrence of fresh fatty changes in other parts of the cord alongside the typical sclerotic lesions.

Analogous lesions to these are found, in the glosso-labio-pharyngeal cases, in the cells of the hypoglossal, facial, motor trigeminal, and finally the pneumogastric nuclei, together with a sclerosis of the anterior pyramids. Essential changes are rarely found above the level of the pons. Thus, at a given level, both the whole of the spinomuscular motor path and the lower portion of the corresponding corticospinal motor path are affected.

ACUTE ANTERIOR POLIOMYELITIS.

Acute anterior poliomyelitis is a disease characteristically found in children. Its healed results are seen in cases of infantile spinal palsy. The process, when caught early, is found to be a true inflammation of the region of the anterior horns, preferably of the cervical and lumbar enlargements of the cord.

Too few cases have been examined early to warrant saying which organism is the most frequent cause. Cases examined at various stages later in the disease show, first, fatty degeneration (Marchi), later, scleroses demonstrable by Weigert's myelin sheath method. Finally a stationary stage is reached in which a certain amount of atrophy in one or both anterior horns can be grossly demonstrated, and a reduction in number of motor cells with gliosis can be made out microscopically.

COMBINED SYSTEM DISEASE.

A peculiar though varying set of symptoms sometimes occurs in pernicious anemia. The same symptoms and the same findings certainly also occur in cases which are not pernicious anemia. The beginnings of the disease have never been microscopically observed. The spinal cord simulates a combination of tabes with degeneration of the pyramidal tracts: thus the posterior columns and the direct cerebellar tract are degenerated, as well as the crossed and sometimes the direct pyramidal tracts.

The symptoms cannot be a mere combination of tabetic and spastic paretic phenomena, for some of these are contradictory. As a fact, according to the distribution and intensity of the lesion, two types of symptoms are found. In the first place, the motor weakness with increase of tonus (spastic paralysis) may be combined with various tabetic symptoms, such as ataxia, lancinating pains, Argyll-Robertson pupil. Or, in the second place, the picture may be predominantly that of tabes, with a motor weakness not found in tabes.

A disease exhibiting somewhat the same distribution of degeneration in the cord (degeneration of Goll's and Burdach's tracts, of Clarke's gray column and the direct cerebellar tract, together with degeneration of the crossed pyramidal tract), besides in certain cases atrophy of the cerebellum, is known as *hereditary ataxia* (Friedreich's disease).

MULTIPLE DISSEMINATED SCLEROSIS.

Young adults, after acute infectious diseases and metal poisoning, or apparently spontaneously, sometimes develop a striking clinical picture: weakness and rigidity of legs, spastic paretic gait with "cerebellar" reeling, tremors attending and increasing with voluntary movements ("intention tremor"), nystagmus (especially on looking sidewise), partial optic atrophy, "scanning" or "syllabic" speech, paroxysmal involuntary laughter, and weakening of intelligence.

To account for these phenomena the central nervous system shows multiple areas of degeneration, which in Weigert myelin sheath preparations are quite sharply demarkated through absence of myelin from surrounding areas. In glia preparations the areas are by no means so sharply marked. Many axis cylinders are preserved in the midst of the fibrillary overgrowth of glia.

SYRINGOMYELIA.

Persons in middle life may notice vesicles on the skin of the hands which fail to heal well. Slight wounds become easily produced. The small muscles of the hand atrophy; the interosseous spaces deepen; fibrillary tremors, "claw hand," and the picture of progressive muscular atrophy develop. The physician may be the first to detect a peculiar disorder of sensibility; whereas the sensations of touch, pressure, and position are intact, the sensations of pain and temperature are lost or decreased over wide areas (*dissociation of symptoms*).

The clinical picture is typical only because of the usual site of the fusiform glia-lined cavity, asymmetrically set, as a rule, a little posteriorly in the central gray of the cervical cord. A condition histologically exactly similar but of different site would produce a quite different picture. The clinical picture is as characteristic and definite as many of those in the system diseases, but the process is not a tract disease.

GENERAL PARESIS.

The brains of some subjects exhibit a characteristic set of changes: the pia mater is thickened almost diffusely and may be edematous; the convolutions are narrowed over limited but wide areas, and the sulci are flaring; small bits of the cortical substance may cling to the pia on peeling; on section the minute cortical vessels stand out prominently. Notwithstanding the absence of arteriosclerosis, there is likely to be a moderate internal hydrocephalus and marked granular ependymitis. Microscopically the cortical vessels attract attention from the infiltration of their sheaths with lymphoid and many plasma cells. The neuroglia shows many phases of overgrowth. The swelling of the neuroglia cell bodies may be determined in regions where defined nerve cell changes are still absent. In many areas the nerve cells exhibit changes of many grades up to replacement. Their regular radial arrangement in the cortex is disturbed. The regular rows of neuroglia cells in the white matter are thrown into disorder by the loss of medullated fibers and the irregular contraction of the intercellular substance.

If the records of the subject be examined, it may be found that syphilis had occurred many (five to twenty) years before. The symptoms which have led to death had begun insidiously two or three years before: a change of character (*e.g.*, from grave to gay or contrariwise) with moral and intellectual impairment and loss of memory. The disease then progresses to graver impairment in which speech disturbance and paralytic attacks are prominent. The pupils show the Argyll-Robertson sign as a rule.

GENERAL DISTRIBUTION OF MUSCULAR PARALYSES AND ATROPHIES.

The distribution of muscular paralyses and atrophies varies with the site of the lesion which produces them. This distribution follows one of four types:

I. Peripheral.
II. Radicular.
III. Medullary and spinal.
IV. Cerebral.

Paralyses and atrophies of peripheral origin are grouped according to the anatomical distribution of the nerves or plexuses involved by lesion. Trauma or pressure may produce effects strictly limited to certain muscle groups. Infectious or toxic injuries to the peripheral nerves produce effects, as a rule, more marked distally (as in the hand or foot).

The radicular paralyses and atrophies ensue upon lesion of the anterior roots and of the trunks of origin in the great plexuses. Almost all the muscles are innervated by fibers in at least two anterior roots. The trunks of origin of the cervical, brachial, lumbar, and sacral plexuses already contain an admixture of sensory with the motor fibers: the paralyses and atrophies of radicular origin are therefore attended by sensory disorders of similar strict localization.

With respect to the myelopathic paralyses and atrophies, which ensue upon lesion of the pyramidal tracts and of the anterior horns respectively, the weight of evidence at present indicates that they follow in general the radicular distribution. Other types of distribution are logically possible and have at various times been assumed, such as a limited distribution with a given nucleus for a given muscle group, or a segmentary (metameric) distribution, or a more diffuse distribution of non-radicular type. The radicular type of distribution is demonstrated well at times in cases of syringomyelia, hematomyelia, and acute anterior poliomyelitis, but may be less distinctly seen in diseases of a more diffuse extent, as in amyotrophic lateral sclerosis, wherein the paralysis and atrophy follow a double lesion of pyramidal tracts and anterior horns.

The distribution of paralyses of cortical origin is rarely as sharply limited as the distribution of muscular contractions excited electrically at the cortex. The lesions are almost without exception too extensive for such focal results; and results less gross than a hemiplegia or a monoplegia are rare in cortical lesions, and still rarer in subcortical or capsular lesions. The muscle groups which subserve the more specialized functions are more apt to be incurably involved in these lesions than the muscles of lower function.

V. THE NEURONE THEORY.

Waldeyer, 1891, offered the following definition of the nervous system: The nervous system is a collection of units which are anatomically and developmentally distinct. Each unit or neurone is composed of three parts, namely, of a nerve cell, a nerve fiber, and a terminal arborization. Conduction proceeds in some neurones from cell to arborization, but in other neurones from arborization to cell. Thus motor impulses are conveyed from cell to arborization, but sensory impulses, on the other hand, run one way in some instances, but in other instances go contrariwise (note, for example, the directions of impulse in the processes of the cells of the dorsal root ganglia).

Waldeyer's definition took its rise from the data of the silver impregnation methods of Golgi, and particularly from Ramón y Cajal's demonstration that the nerve cells of embryos and fetuses throw out processes which all end blindly. However, it has never been so clear that the nerve cells of the adult invariably remain anatomically distinct. Edinger and others have held that although there must remain a doubt whether the processes are continuous or only contiguous, nevertheless the neurone must be maintained as a biologically independent unit.

The neurone theory has thus undergone various changes since its first exposition. The most frequent insistence is made upon the trophic nature of its function. An explanation seems demanded for the data of Wallerian degeneration and the invariable results of the method of Gudden. Thus, if destruction of a given gray center or section of a given nerve bundle constantly produces retrograde changes in certain remote circumscribed foci and the connecting paths, it is certainly possible to regard the cells involved as neurones, as units having a functional value and unity, whose anatomical nature may be left out of account.

Many of the tract diseases sketched above are neatly interpretable in terms of the neurone theory. Thus, the pyramidal tract may be considered to be a bundle of fibers belonging to the *corticospinal neurone system.* The corticospinal neurone system may be said to come into relation in the anterior horns with a peripheral or *spinomuscular neurone system.* Further, to take up the sensory half of the loop made by the projection system, the apparatus connecting sensory end organs with higher centers, which consists for the spinal cord of the dorsal root ganglia, the sensory peripheral nerves and the columns of Goll and Burdach may be termed the *gangliospinal neurone system.* The central (intraspinal) tracts of the gangliospinal neurone system come into relation with new ascending neurone systems in the medulla (*bulbocentral neurone systems*), of which we suppose, on account of the rapid playing out of degeneration tracts at higher levels, there is an end-to-end series. Moreover the direct cerebellar tract, which becomes degenerate on section of the thoracic cord, may, in conjunction with the cells of Clarke's column from which it takes its rise, be regarded as a fresh neurone system, a *spinocerebellar neurone system.*

In a certain series of diseases (secondary degenerations, tabes dorsalis, anterior poliomyelitis, and so on) these neurone systems undergo changes as units. In some of the diseases our attention has been directed by this consideration to look for changes in the gray centers which might otherwise have been overlooked. It would be oversanguine to assume that actual progress in making clear the facts has been accomplished by the neurone hypothesis. In so far as it restates facts and discoveries made in most cases without its use, the hypothesis may be assigned a limited value. But the true cause of the so-called primary degeneration remains remote from us. It remains mysterious why the intraspinal portion of the gangliospinal neurone system is chiefly affected in tabes, why in amyotrophic lateral sclerosis and in progressive muscular atrophy (if they are separate diseases) the spinomuscular neurone and a portion of the corticospinal neurone are affected, and why the process in anterior poliomyelitis should sometimes be confined to the spinomuscular neurone system and sometimes involve also the direct cerebellar tract. In the latter case it is probable that the simple explanation suffices that in some cases the acute inflammatory process is at the outset more extensive than in other cases.

The neurone terminology is now widespread and is harmless, so long as the tendency does not grow of supposing certain diseases to grow spontaneously out of the unitary structure of the neurone. The neurone theory is an interesting restatement which explains nothing as to the nature of diseases peculiar to the nervous system, but may sometimes give hints as to their extent.

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